Chapter

Introductory Chapter: Stem Cells - Do We Really Know Everything Already?

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1. Introduction

The current trend in medicine divides into two aspects of treatment - preventive medicine and regeneration of damaged tissues (regenerative medicine) [1]. One of goals of regenerative medicine is to improve wound healing without major surgical procedures and donor-site morbidity. This may be obtained by cell-based therapy [2]. The potential to restore tissue to its pre-injured state may be achieved by novel therapeutic modalities, including stem cells. Stem cells have been proposed for the treatment and management of variety of diseases in recent years. In PubMed 366,445 results occur when stem cells phrase is searched, including 5,547 publications describing clinical trials (**Figure 1**).

2. Current knowledge

There is still much to know about stem cells. How they differentiate? Why some therapies may not be effective? How can we use stem cells in other way? Latest studies shown that shape change may be indicator of cell's exit from pluripotency and prevention of release cell membrane from actin cortex may prevent cells from differentiation [3]. It is know that microenvironment impact cells responses which direct tissue growth and physiology [4]. Influencing cell responsiveness may

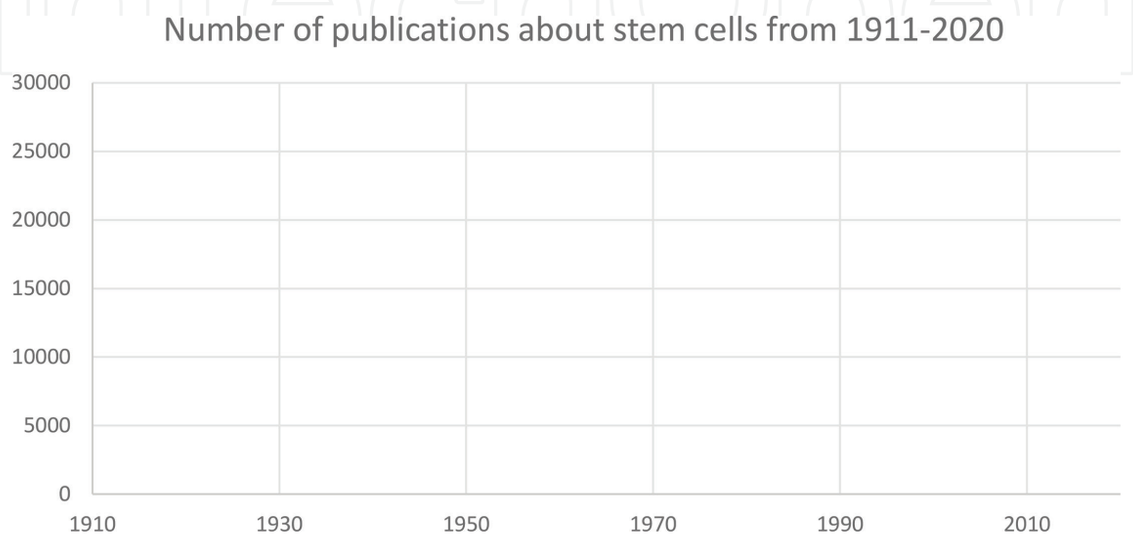

Figure 1.
Stem cell studies and research development during over 100 years.

enhance the regenerative potential of stem cells and therefore improve therapies. Combination of mechanobiological factors can support MSCs to promote vascular regeneration, enhancing endogenous regeneration differentiating them to cell types crutial in neoangiogenesis [5]. But may stem cells be answer in whole organs regeneration or transplantation? Organoids, which are multicellular structures consisting of organ-specific cells are widely created not only to understand organogenesis and disease progression but also in order to potentially treat organ failure [6]. Unfortunately obtaining full organ from stem cells will be impossible for next few decades as organoids made from stem cells are highly simplified [7]. However in other clinical fields stem cells therapies has been widely used for many years.

3. The source

The sources of stem cells for different therapies may vary. Different types of stem and progenitor cells can be isolated from different perinatal tissues, making them particularly interesting candidates for use in cell therapy and regenerative medicine. The main source of perinatal stem cells is cord blood. Cord blood has been a well-known source of hematopoietic stem/progenitor cells since 1974. For over 30 years, umbilical cord blood obtained from biobanks has been used in the treatment of various hematological and immune disorders. Other perinatal tissues that are routinely discarded as medical waste contain non-hematopoietic cells of potential therapeutic value. Indeed, mesenchymal stromal cells are most commonly used in advanced research into perinatal cell therapy [8]. In this perspective, the placenta may deserve special attention [9]. The placenta is a temporary organ that is ejected after birth and is one of the most promising sources of various cells and tissues for use in regenerative medicine and tissue engineering, both experimental and clinical. The placenta has unique intrinsic features because it plays many roles during pregnancy: it is formed by the cells of two people (mother and fetus), contributes to the development and growth of an allogeneic fetus, and has two independent and interacting circulatory systems [8, 9]. The application of MSCs isolated from the amniotic membrane on the acelular dermal matrix ADM allowed for complete healing of extensive wounds of the burned patient without the need to perform an autologous skin transplant [10] which may be a game changer in burn treatment therapy.

4. Clinical applicability

Stem cells are used not only to support wound healing. Stem cells transplantation in patients with multiple sclerosis and amyotrophic lateral sclerosis was a clinically feasible and relatively safe procedure that produces an immediate immunomodulatory effect [11]. Interesting results for the treatment of autism were presented in an open-label Phase I trial. Ongoing inflammation of the nervous system may contribute to the symptoms of autism spectrum disorder (ASD). Mesenchymal stromal cells (MSCs) have been shown to modulate inflammation in the nervous system [12]. Another interesting application of MSCs may be in the future the use of their potential to modulate the immune response during immunosuppressive therapy. Stem cells have been shown to modulate the action of immunosuppressants, and when combined with immunosuppressants, they have a pronounced effect on cell activation and the balance between different T cell subpopulations and exert an inhibitory effect on pro-inflammatory T cell subsets while promoting anti-inflammatory Treg cell function. MSC-based therapy has been shown to be a

powerful strategy to mitigate the negative effects of immunosuppressive drugs on the immune system [13]. Those therapies may cause concern about safety but many clinical trials has been studying the safeness and efficacy of mesenchymal stem cells therapies. Most recent describes Phase 1 trial for treatment of COVID-19 patients with pulmonary fibrosis using hESC-IMRCs [14] in which none of the treated patients suffered any adverse events or abnormal responses related to cell therapy. This suggest that stem cell therapies has become more and more safe, popular and researchers discover every year new potential fields of treatment with usage of stem cells.

5. Possibilities

Where else stem cells can be used if not for transplantation? Another option is to study evolutionarily conserved mechanisms with usage of interspecies pluripotent stem cell (PSC) co-culture. This mode enables uncovered a unknown competitive cell interaction during early mammalian development [15].

Stem cells show ourselves many possibilities and when we start think that we know already something a whole new branch of research opens thanks to this unique cells. This book guides us through stem cell types, therapy possibilities, law and ethical aspects. It is complete source of knowledge which is base of further research.

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